ISSN 1070-3632, Russian Journal of General Chemistry, 2015, Vol. 85, No. 12, pp. 2853–2860. © Pleiades Publishing, Ltd., 2015.

Design and Synthesis of Novel Fused Heterocycles Using 4-Chromanone as Synthon[1]

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Received August 7, 2015

Abstract—A new series of heterocyclic systems, including azole, azolopyrimidine, and pyridopyrimidine derivatives, attached to 2*H*-chromene scaffold, was prepared by a convenient procedure through the reactions of (*E*)-2-dimethylamino-methylene chromanone with different nitrogen binucleophiles. Various substituted chromeno[4,3-*b*]pyridine derivatives were also prepared through the reactions of (*E*)-2-dimethylamino-methylene chromanone with a series of active methylene compounds.

Keywords: 4-chromanone, pyrazole, pyrimidine, pyridine

DOI: 10.1134/S107036321512035X

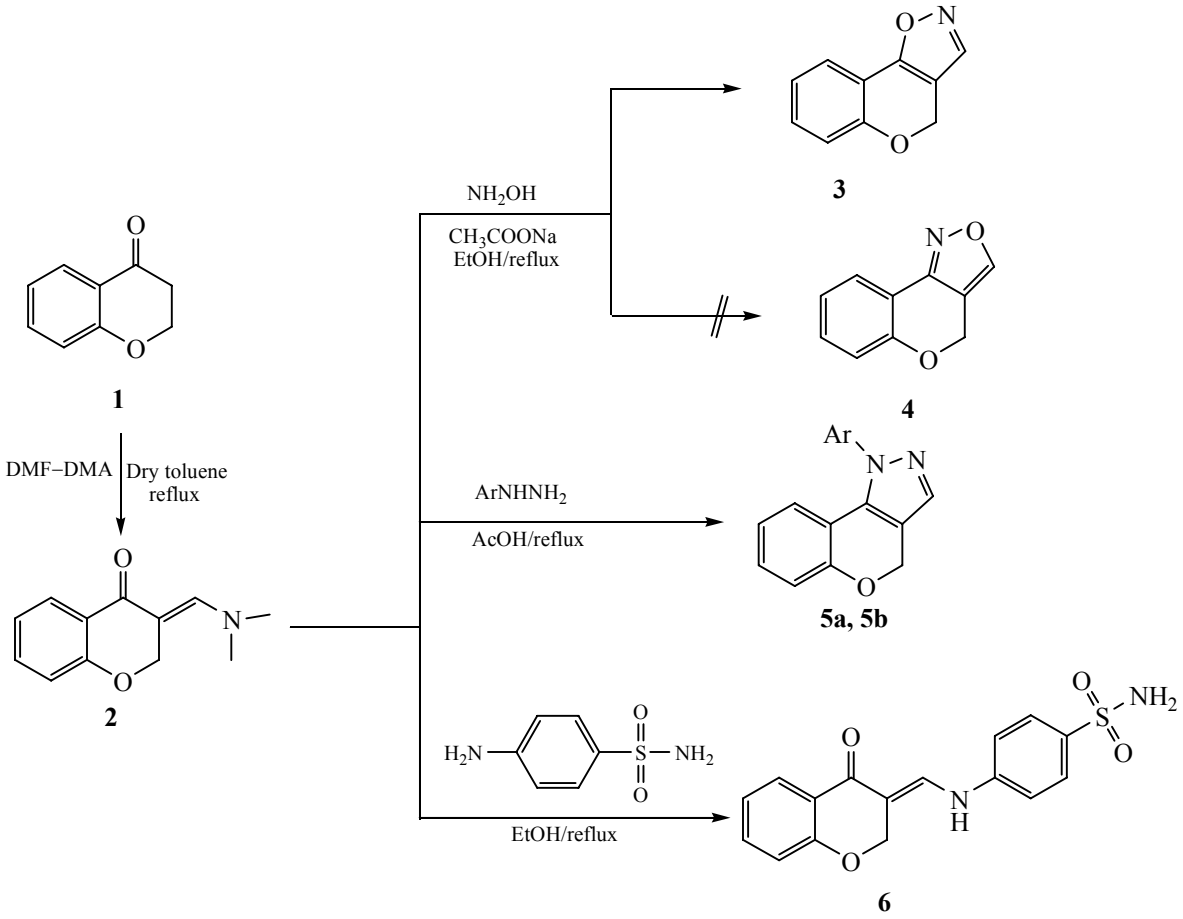
Enaminone derivatives are highly reactive intermediates and their utility for preparation of important heterocycles has recently gained considerable interest [1–3]. On the other hand, chromenes are important medicinal pharmacophores found in many important natural products, such as flavonoids, tocopherols, anthocyanins, and natural alkaloids [4]. Chromene derivatives also possess interesting biological activities, such as anti-inflammatory, antivascular, antitumor, antibacterial, antifungal, and antitubercular activity [5–7]. In continuation of our recent studies [8–14] aiming at the development of new and simple methods for the synthesis of a variety of biologically important heterocyclic ring systems, we report herein a facile route to synthesize various pyrazoles, isoxazoles, pyrimidines, pyrazolopyrimidines, triazolopyrimidines, and pyridines as fused with chromene scaffold.

(*E*)-2-Dimethylamino methylenechromanone **2**, assignable as *E*-configuration [15], was prepared by the reaction of chroman-4-one (**1**) with dimethylformamide dimethyl acetal (DMF–DMA) in refluxing dry toluene [16]. The treatment of enaminone **2** with hydroxylamine hydrochloride in the presence of anhydrous sodium acetate gave 4*H*-chromeno[4,3-*c*]-isoxazole (**3**), rather than the isomeric form **4**. The ^{1}H NMR spectrum of the compound **3** has signal of isoxazole H^3 protons at 8.33 ppm. The formation of the isomeric product **4** was excluded, because the isoxazole H^5 protons resonate at downfield around δ 9.30 ppm [17, 18]. Enaminone **2** was reacted with arylhydrazines in glacial acetic acid under reflux temperature to give 1,4-dihydro-1-aryll chromeno[4,3-*c*]pyrazole (**5a, 5b**). The ^{1}H NMR spectrum of compound **5a** has signal at 7.55 ppm, a characteristic of pyrazole H^3. The treatment of enaminone **2** with 4-aminobenzenesulfonamide under reflux condition yielded (*E*)-4-[4-oxo-2*H*-chromen-3(4*H*-ylidene)methyl-amino]benzenesulfonamide (**6**) (Scheme 1).

The treatment of enaminone **2** with 4*H*-1,2,4-triazol-3-amine **7** or 2-amino benzimidazole **9** in refluxing glacial acetic acid always gave a single product, which was identified as 6*H*-chromeno[3,4-*e*][1,2,4]triazolo-[1,5-*a*]pyrimidine (**10**) and (*E*)-3-[(1*H*-benzo[*d*]imidazol-2-ylamino)methylene]-2,3-dihydrochromen-4-one (**12**) respectively. ^{1}H NMR spectrum of the compound **10** has signals at 8.59 and 8.63 ppm, a characteristic of triazole-*H* and pyrimidine-*H*, respectively, signals at 5.36 ppm, and multiplet signals at δ = 7.07–7.89 ppm, which are due to CH_2 and phenyl protons, respectively. The reaction of aminotriazole **7** with enaminone **2** is

[1] The text was submitted by the authors in English.

Scheme 1. Synthetic pathway for the formation of compounds **3**, **5a**, **5b**, and **6**.



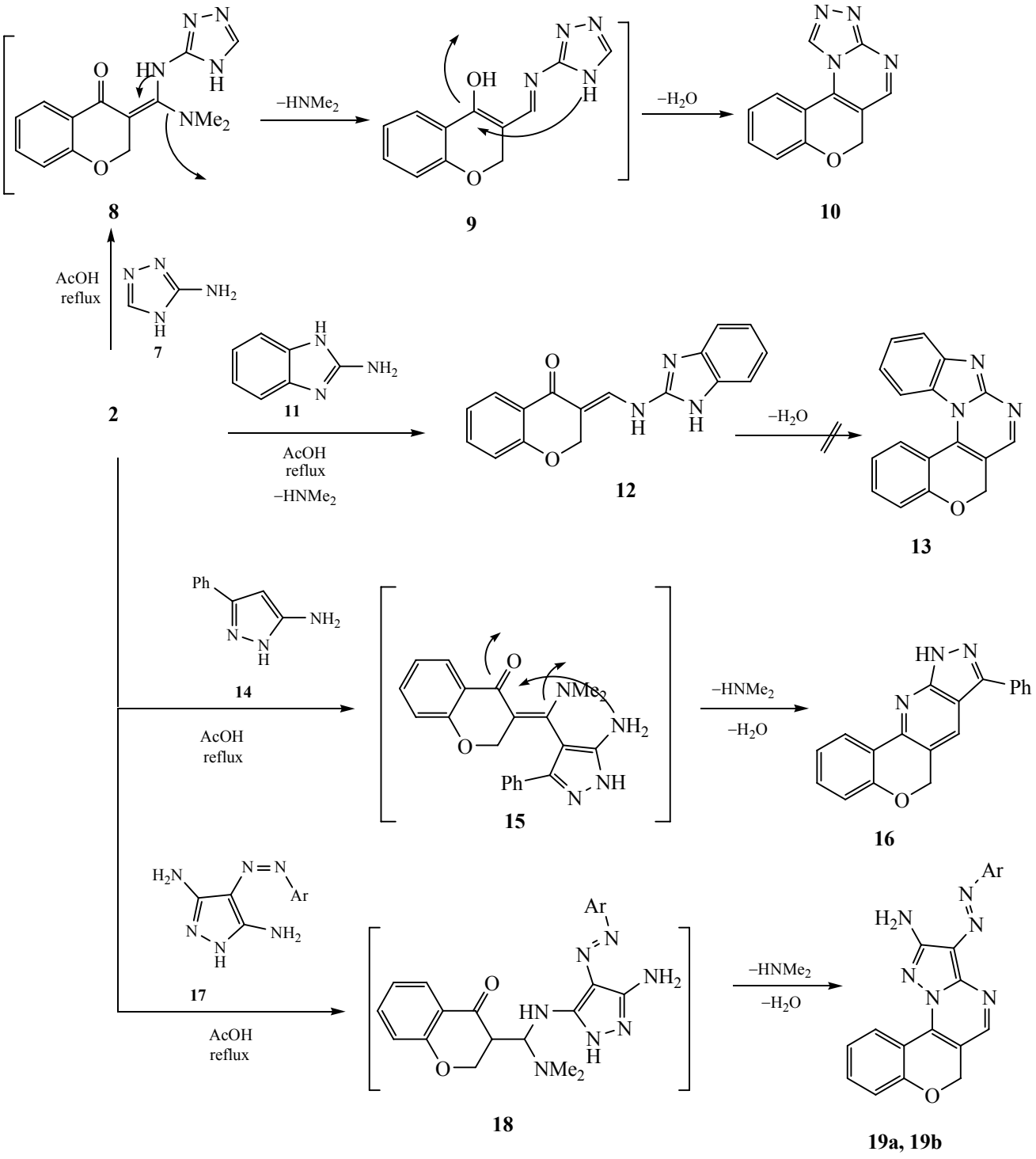
Ar =Ph (**a**), Ar = 2,4-$(NO_2)_2C_6H_3$ (**b**).

assumed to proceed via the initial Michael addition of the exo-amino group of the amine to the enamine double bond. The resulting product is a nonisolable intermediate **8**, which undergoes the intramolecular oxidative cyclization with the elimination of the dimethyl amine and water molecules to give a compound **10**. The reaction of enaminone **2** with 2-aminobenzimidazole was sterically hindered at the stage of formation of a compound **12** (Scheme 2).

The treatment of enaminone **2** with 5-amino-3-phenyl-1*H*-pyrazole **14** and 4-(aryldiazo)-1*H*-pyrazole-3,5-diamine **17a, 17b** in refluxing acetic acid gives the condensed pyrazolopyridine and pyrazolopyrimidine derivatives, compounds **16** and **19a, 19b**, respectively. The reaction of enaminone **2** with 5-amino-1*H*-pyrazole **14** is assumed to proceed via the initial C-nucleophilic addition of pyrazole-CH in **14** to the enamine double bond in **2** to form a nonisolable intermediate **15,** which undergoes intramolecular oxidative cyclization and aromatization via the loss of both dimethylamine and water molecules to yield a compound **16** (Scheme 2).

2(*E*)-2-dimethylaminomethylenechromanone **2** was reacted with 6-amino-2 thioxopyrimidin-4-one **20** in boiling acetic acid. The progress of the reaction was monitored by thin-layer chromatography (TLC), which showed that after 6 h the conversion of the starting material was complete. ^{1}H NMR spectrum of the crude mixture gave good evidence for the presence of two products, **21** and **22**, which were isolated by several crystallizations (Scheme 3). ^{1}H NMR spectrum of compound **21** has signals at 12.5 and 13.1 ppm, a characteristic of 2NH (pyrimidine NH) and singlet signal of the pyridine-4*H* proton at 8.18 ppm, which is in agreement with the structure **21** [18]. 1,3-Diketones, β-keto esters, and β-ketonitriles are compounds of special interest in organic synthesis. They may be used

Scheme 2. Synthetic pathway for the formation of compounds **10, 12, 16, 19a, 19b**.

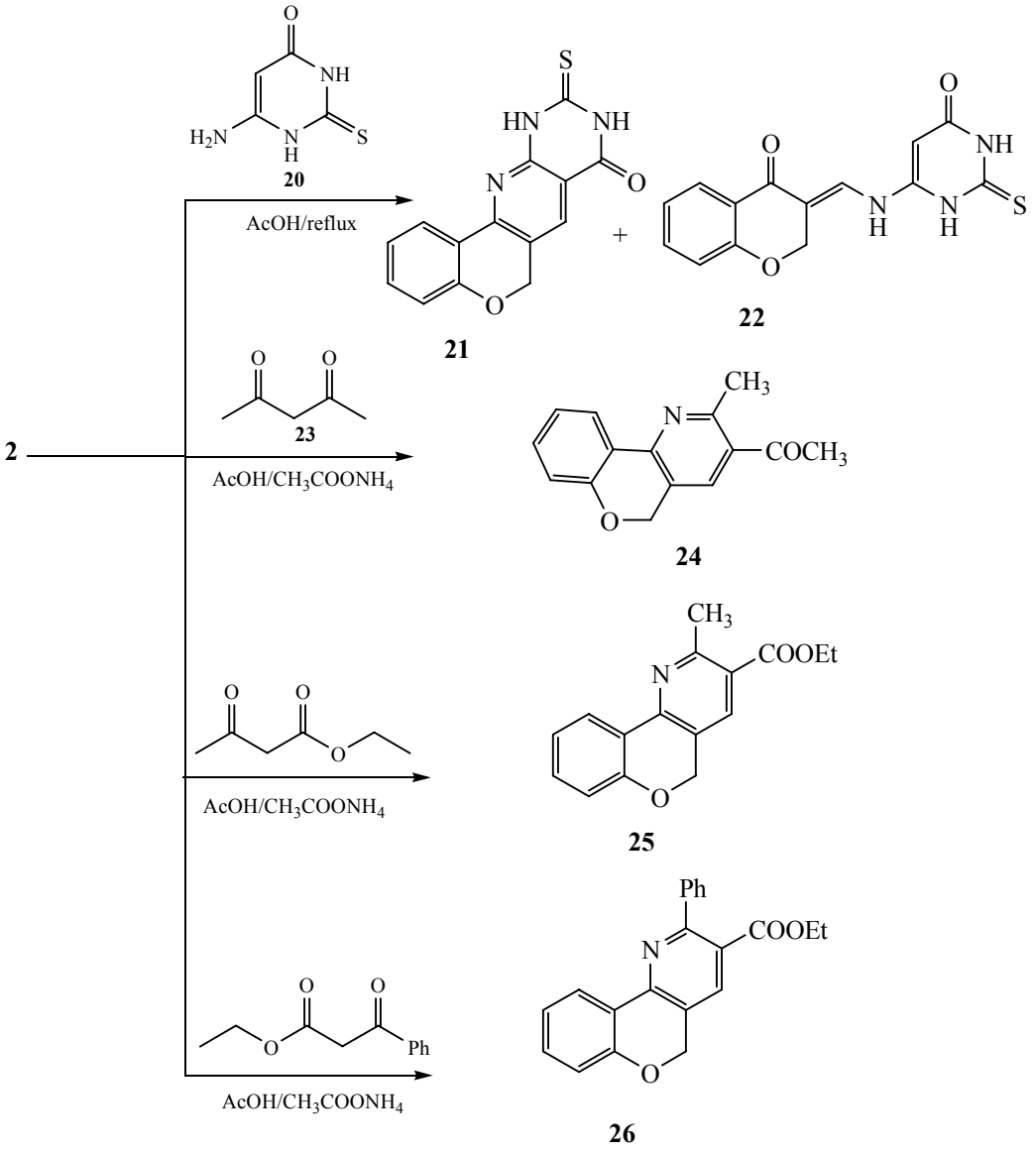


Ar =Ph (**a**), Ar = *p*-Cl–Ph (**b**).

for the preparation of biologically active ingredients as multi-functional building blocks and for the formation of fused pyridines as key reagents [19].

Treatment of enaminone **2** with acetyl acetone, ethyl acetoacetate, and ethyl benzoyl acetate in glacial acetic acid in the presence of ammonium acetate gives

Scheme 3. Synthetic pathway for the formation of compounds **21, 22, 24–26.**



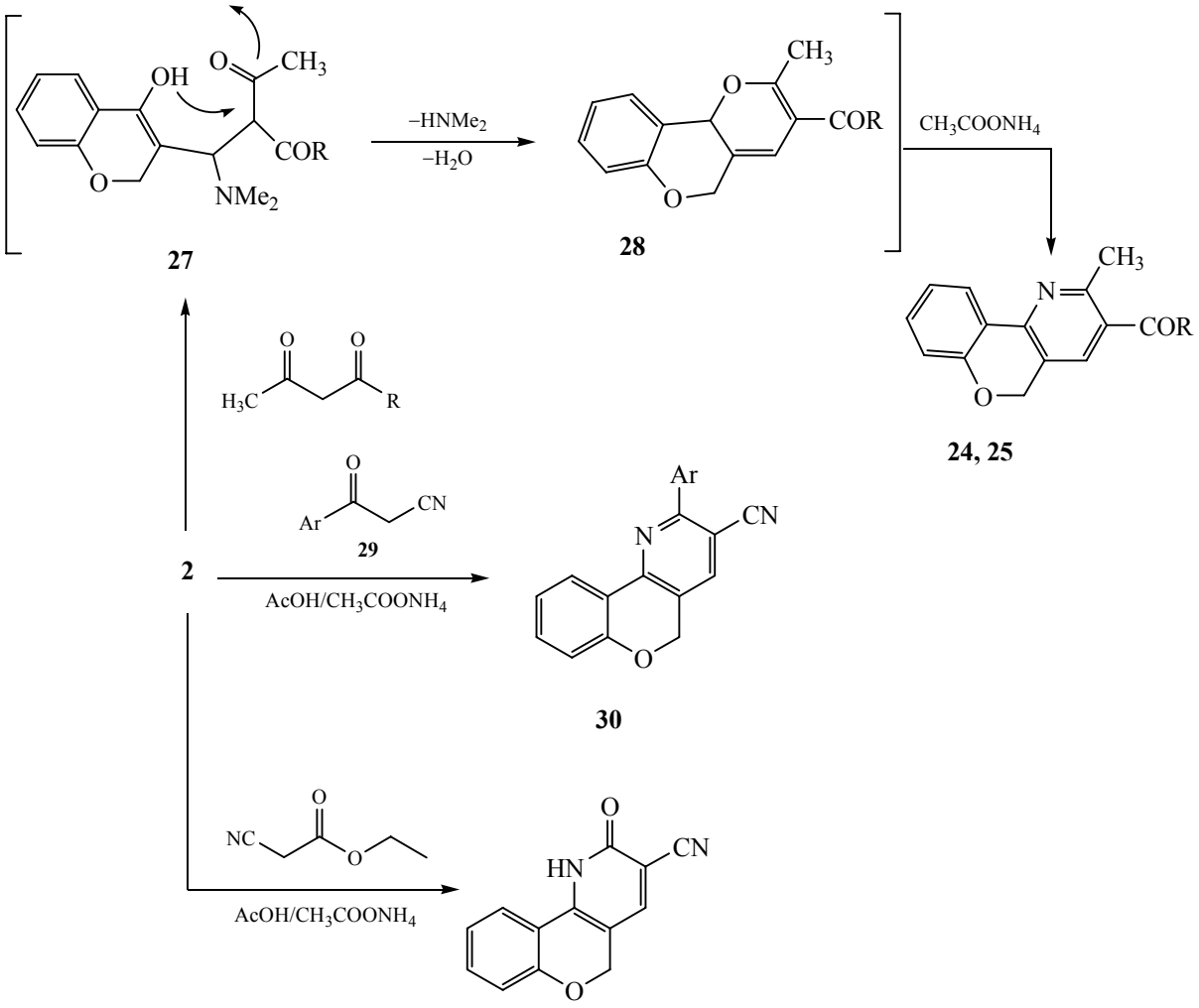
chromeno[4,3-*b*]pyridine derivatives **24**–**26**, respectively (Scheme 3). The ^{1}H NMR spectra have signals at 8.31, 8.27, and 8.21 ppm, a characteristic of the pyridine-4*H* protons of compounds **24**–**26,** respectively.

Finally, 2-(4-chlorophenyl)-5*H*-chromeno[4,3-*b*]pyridine-3-carbonitrile (**30**) and 2,5-dihydro-2-oxo-1*H*-chromeno[4,3-*b*]pyridine-3-carbonitrile (**31**) were formed by the reaction of enaminone **2** with benzoyl acetonitrile derivative **29** and ethyl 2-cyanoacetate, respectively (Scheme 4).

EXPERIMENTAL

The melting points were measured on an Electro thermal IA 9000 series digital melting point apparatus. The IR spectra of samples (discs pressed with potassium bromide) were recorded on a Pye Unicam SP 3300 and a Shimadzu FT IR 8101 PC infrared spectrophotometers. The 1H NMR spectra were measured on a Varian Mercury VXR-500 MHz spectrometer. Chemical shifts δ are given in ppm downfield from tetramethylsilane (TMS) used as

Scheme 4. Synthetic pathway for the formation of compounds **30** and **31**.



Ar = Ph/4-Cl.

internal standard. ^{1}H NMR (500 MHz) and ^{13}C NMR (125 MHz) spectra were run in deuterated chloroform ($CDCl_3$) or dimethylsulphoxide (DMSO-d_6). Mass spectra were recorded on a Shimadzu GCMS-QP1000 EX mass spectrometer at 70 eV. Elemental analysis was carried out at the Microanalytical Centre of the Cairo University, Giza, Egypt. All reactions were monitored by thin-layer chromatography (Silica gel, Aluminum Sheets 60 F254, Merck). Compounds **14** [20], **17** [21], **19** [22], and **20** [23] were prepared according to the literature procedures.

Synthesis of (*E*)-3-[(dimethylamino)methylene]-2,3-dihydrochromen-4-one (2). A mixture of 2,3-dihydrochromen-4-one (**1**) (1.49 g, 10 mmol) and dimethylformamide dimethylacetal (DMF–DMA) (1.33 mL, 10 mmol) in toluene (20 mL) was refluxed for 10 h. After cooling, the solvent was evaporated under reduced pressure and the obtained product was ground with ether into the powder to form the solid product **2** in the form of pale yellow crystals. An analytically pure sample was obtained by crystallization with EtOH. Yield (1.61 g, 85%), mp: 138–139°C [15]. IR spectrum, ν, cm^{-1}: 1680 (C=O). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.16 s (6H, $2CH_3$), 5.62 s (2H, CH_2), 6.9 d, 7.95 d (2H, ArH) 7.45 s (1H, CH=C), 7.03 t, 7.37 t (2H, ArH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 43.85, 66.95, 99.62, 116.590, 121.36, 123.79, 127.43, 133.68, 148.27, 160.30, 181.83. Mass spectrum: *m/z* 203 (40%). Calculated, %: C 70.92; H 6.45; N 6.89.

$C_{12}H_{13}NO_2$. Found, %: C 70.85; H 6.57; N 6.80. *M* 203.24.

Preparation of 4*H*-chromeno[4,3-*c*]isoxazole (3). To a mixture of the enaminone **2** (0.2 g, 1 mmol) and hydroxylamine hydrochloride (0.07g, 1 mmol) in EtOH (10 mL) anhydrous sodium acetate (0.82 g, 1 mmol) was added. The reaction mixture was refluxed for 5 h, cooled, and then diluted with water (30 mL). The formed precipitate was collected by filtration, washed with water, dried, and recrystallized from EtOH to give 4*H*-chromeno[4,3-*c*]isoxazole (compound **3**). Yield (0.11 g, 64%); white ppt (EtOH), mp 130–131°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 5.6 s (2H, CH_2), 7.48–8.0 m (4H, ArH), 8.33 s (1H, CH-isoxazole). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 67.11, 93.53, 116.73, 116.96, 121.64, 124.07, 128.58, 145.97, 157.40, 157.51. Mass spectrum: *m/z* 173 (5%). Calculated, %: C 69.36; H 4.07; N 8.09. $C_{10}H_7NO_2$. Found, %: C 69.25; H 4.22; N 8.19. *M* 173.17.

Synthesis of 1,4-dihydro-1-(arylchromeno[4,3-*c*]-pyrazole (5a, 5b). To a solution of the enaminone **2** (0.2 g, 1 mmol) in glacial acetic acid (10 mL), the appropriate aryl hydrazine (1 mmol) was added. The reaction mixture was heated under reflux for 4–6 h, cooled, and poured into an ice-cold solution of sodium bicarbonate. The separated solid was filtered off, repeatedly washed with water, dried, and recrystallized from EtOH to give the corresponding pyrazole derivative **5a, 5b**.

1,4-Dihydro-1-phenylchromeno[4,3-*c*]pyrazole (5a). Yield (0.18 g, 72%); pale yellow crystals (EtOH), mp 140–142°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: ^{1}H NMR spectrum, δ, ppm: 5.28 s (2H, CH_2), 6.75–7.14 m (4H, ArH) 7.48–7.52 m (5H, ArH), 7.55 s (1H, CH-pyrazole). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 61.28, 114.63, 116.22, 117.74, 121.44, 122.65, 125.39, 128.81, 129.38, 129.52, 133.71, 134.83, 140.34, 153.90. Mass spectrum: *m/z* 248 (100%). Calculated, %: C 77.40; H 4.87; N 11.28. $C_{16}H_{12}N_2O$. Found, %: C 77.57; H 4.95; N 11.35. *M* 248.28.

1,4-Dihydro-1-(2,4-dinitro-phenyl)chromeno-[4,3-*c*]pyrazole (5b). Yield (0.25 g, 75%); pale yellow crystals (EtOH), mp 161–162°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 5.5 s (2H, CH_2), 7.17–7.60 m (4H, Ar-H), 7.86 s (1H, CH-pyrazole), 7.87 d, 8.54 d (2H, ArH), 9.33 s (1H, Ar-H). Mass spectrum: *m/z* 338 (100%). Calculated, %: C 56.81; H 2.98; N 16.56. $C_{16}H_{10}N_4O_5$. Found, %: C 56.74; H 2.89; N 16.48. *M* 338.27.

Synthesis of (*E*)-3-[(4-aminophenylsulfonamido-amino)methylene]chroman-4-one (6). To a solution of enaminone **2** (0.2 g, 1 mmol) in EtOH (10 mL), *p*-amino benzene sulfonamide (0.17 g, 1 mmol) was added. The reaction mixture was heated under reflux for 8 h. The solvent was distilled off under reduced pressure and the residual brown solid was recrystallized from ethanol to form a compound **6**. Yield (0.28g, 84%); pale yellow crystals (EtOH), mp 270–272°C. IR spectrum, ν, cm^{-1}: 3360, 3161 (NH, NH_2), 1644 (C=O). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 4.15 s (2H, CH_2), 6.72 s (2H, NH_2-SO_2, D_2O-exchangeable), 6.68–7.82 m (8H, ArH) 8.09 d (1H, CH-enamine), 8.5 d (1H, NH, D_2O-exchangeable). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 40.35, 111.68, 112.91, 118.92, 121.09, 123.25, 125.41, 127.83, 131.10, 134.71, 151.34, 154.91, 156.42, 176.83. Mass spectrum: *m/z* 330 (15%). Calculated, %: C 58.17; H 4.27; N 8.48. $C_{16}H_{14}N_2O_4S$. Found, %: C 58.25; H 4.33; N 8.41. *M* 330.36.

Synthesis of compounds 10, 12, 16, and 19a, 19b *(general procedure).* A mixture of enaminone **2** (0.2 g, 1 mmol) and the appropriate heterocyclic amines **7**, **9**, **14,** or **17** (1 mmol) in glacial acetic acid (20 mL) was heated under reflux for several hours (the reactions were followed up by TLC). After cooling, the reaction mixture was poured into ice cold water and neutralized with sodium bicarbonate. The solid product was collected by filtration, thoroughly washed with water, dried, and finally recrystallized from EtOH into compounds **10, 12, 16,** and **19a, 19b**, respectively.

6*H*-Chromeno[3,4-*e*][1,3,4]triazolo[1,5-*a*]pyrimidine (10). Yield (0.17 g, 75%); pale yellow crystals (EtOH), mp 195–197°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 5.36 s (2H, CH_2), 7.07–7.89 (m, 4H, ArH), 8.59 s (1H, tiazole-H) and 8.63 s (1H, pyrimidine-H). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 64.72, 112.28, 114.83, 117.64, 122.69, 129.58, 134.71. 138.35, 150.36, 156.20, 156.36. 157.45. Mass spectrum: *m/z* 224 (15%). Calculated, %: C 64.28; H 3.60; N 24.99. $C_{12}H_8N_4O$. Found, %: C 64.15; H 3.48; N 24.85. *M* 224.22.

(*E*)-3-[(1*H*-Benzo[*d*]imidazol-2-ylamino)methylene]-2,3-dihydrochromen-4-one (12). Yield (0.19 g, 69%); yellow crystals (EtOH), mp: 245–248°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 4.97 s (2H, CH_2), 5.24 s (1H, CH-enamine), 6.9–7.75 m (8H, ArH), 9.87 s (1H, NH-enamine), 10.37 s (1H, benzimidazole NH). ^{13}C NMR spectrum (DMSO-d_6), δ_H, ppm: 66.56, 109.58, 117.28, 119.35, 121.31, 121.53, 122.43, 126.76, 127.12, 129.54, 131.49, 133.76, 142.34, 145.0, 148.69, 155.13,

192.34. Mass spectrum: *m/z* 291 (10%). Calculated, %: C 70.09; H 4.50; N 14.42. $C_{17}H_{13}N_3O_2$. Found, %: C 70.19; H 4.62; N 14.32. *M* 291.3.

8-Phenyl-5*H*-chromeno[4,3-b]pyrazolo[4,3-*e*]-pyridine (16). Yield (0.23 g, 79 %); yellow crystals (EtOH), mp 170–172°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 5.26 s (2H, CH_2), 7.05–7.53 m (9H, ArH), 8.07 s (1H, pyridine-4*H*), 9.52 s (1H, NH). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 65.04, 93.62, 110.38, 117.26, 122.27, 126.64, 128.79, 130.24, 132.85, 133.41, 135.88, 145.06, 149.06, 151.42, 156.10, 157.38. Mass spectrum: *m/z* 299 (95%). Calculated, %: C 76.24; H 4.38; N 14.04. $C_{19}H_{13}N_3O$. Found, %: C 76.32; H 4.31; N 14.14. *M* 299.33.

2-Amino-1-(2-phenyldiazenyl)-5*H*-chromeno-[4,3-*e*]pyrazolo[1,5-*a*]pyrimidine (19a). Yield (0.23 g, 67%); orange crystals (EtOH), mp 260–262°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 5.37 s (2H, CH_2), 7.16–7.83 m (9H, ArH), 8.52 s (1H, pyrimidine-*H*). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 64.98, 113.01, 114.66, 115.65, 117.98, 121.63, 122.32, 129.04, 129.59, 130.4, 134.61, 135.16, 146.95, 148.48, 152.47, 153.46, 158.04. Mass spectrum: *m/z* 342 (100%). Calculated, %: C 66.66; H 4.12; N 24.55. $C_{19}H_{14}N_6O$. Found, %: C 66.72; H 4.17; N 24.59. *M* 342.35.

2-Amino-1-[2-(4-chlorophenyl)diazenyl]-5*H*-chromeno[4,3-*e*]pyrazolo[1,5-*a*]pyrimidine (19b). Yield (0.30 g, 79 %); orange crystals (EtOH), mp: 290–292°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 5.08 s (2H, CH_2), 6.98–7.85 m (8H, ArH), 8.15 s (1H, pyrimidine-H). Mass spectrum: *m/z* 376 (100%). Calculated, %: C 60.56; H 3.48; N 22.30. $C_{19}H_{13}ClN_6O$. Found, %: C 60.42; H 3.35; N 22.27. *M* 376.80.

Synthesis of compounds 21, 22. To a solution of **2** (0.2 g, 1 mmol) in acetic acid (10 mL) 6-amino-thiouracil **20** (0.143 g, 1 mmol) was added. The reaction mixture was heated under reflux for 6 h, then concentrated and cooled to room temperature. The solid part was collected by filtration, thoroughly washed with EtOH, and crystallized with EtOH/dioxane into the cyclic product **21.** The liquid part was evaporated under reduced pressure and the resulting solid was then recrystallized with methanol to give 6-{(*E*)-[4-oxo-2*H*-chromen-3(4*H*)-ylidene]methylamino}-2,3-dihydro-2-thioxopyrimidin-4(1*H*)-one (**22**).

1,2,3,4,7-Pentahydro-3-thioxo-chromeno[4',3':4,5]-pyrido[2,3-*d*]pyrimidine-1-one (21). Yield (0.13 g, 45%); orange crystals (EtOH), mp 210–212°C. IR spectrum, ν, cm^{-1}: 3325–3120 (NH), 1680 (C=O). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 5.25 s (2H, CH_2), 7.07–7.43 m (4H, ArH), 8.18 s (1H, pyridine-4H). 12.52 s, 13.1 s (2H, 2NH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 63.45, 111.10, 115.8, 117.33, 121.51, 126.11, 128.12, 131.22, 147.8, 150.11, 152.91, 158.31, 162.01. 172.12. Mass spectrum: *m/z* 283 (100%). Calculated, %: C 59.35; H 3.20; N 14.83. $C_{14}H_9N_3O_2S$. Found, %: C 59.55; H 3.45; N 14.67. *M* 283.31.

6-{(*E*)-[4-Oxo-2*H*-chromen-3(4*H*)-ylidene]methylamino}-2,3-dihydro-2-thioxopyrimidin-4(1*H*)-one (22). Yield (0.1 g, 33%); yellow crystals (EtOH), mp 179–181°C. IR spectrum, ν, cm^{-1}: 3302–3121 (2NH), 1685 (C=O). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 4.21 s (1H, NH-enamine), 5.33 s (2H, CH_2), 6.51 s (1H, CH-enamine), 7.11–7.45 m (4H, ArH), 8.11 s (1H, pyrimidiene-H), 8.8 br.s, 11.51 br.s (2H, pyrimidiene-2NH). ^{13}C NMR spectrum (DMSO-d_6), δ, ppm: 61.21. 72.10, 113.81, 118.11, 121.11, 122.46, 129.81, 132.58, 134.41, 159.11, 161.32, 166.52, 173.21, 184.21. Mass spectrum: *m/z* 301 (75%). Calculated, %: C 55.80; H 3.68; N 13.95. $C_{14}H_{11}N_3O_3S$. Found, %: C 55.89; H 3.73; N 13.85. *M* 301.32.

Synthesis of compounds 24–26, 30, and 31 *(general procedure).* To a mixture of compound **2** (0.2 g, 1 mmol) and ammonium acetate (0.2 g) in glacial acetic acid (10 mL), acetyl acetone, ethyl acetoacetate, ethyl benzoyl acetate, benzoyl acetonitrile **29** or ethyl cyanoacetate (1 mmol) was added. The reaction mixture was heated under reflux for several hours and then poured into a cold solution of sodium bicarbonate. The reaction progress was monitored by TLC. The formed solid products were collected by filtration, washed with water, dried, and recrystallized from the proper solvent to give the pyridine derivatives **24–26, 30,** and **31**, respectively.

1-(2-Methyl-5*H*-chromeno[4,3-*b*]pyridin-3-yl)-ethanone (24). Yield (0.18 g, 75%); colorless crystal (EtOH), mp 115–117°C; IR spectrum, ν, cm^{-1}: 1685 (C=O). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.64 s, 2.84 s (6H, $2CH_3$), 5.4 s (2H, CH_2), 6.99–7.74 m (4H, ArH), 8.31 s (1H, CH-pyridine). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 25.23, 29.36, 67.51, 117.11, 122.44, 122.51, 122.79, 125.34, 131.93, 132.27, 133.23, 150.01, 156.59, 158.52, 199.47. Mass spectrum: *m/z* 239 (100%). Calculated, %: C 75.30; H 5.48; N 5.85. $C_{15}H_{13}NO_2$. Found, %: C 75.43; H 5.55; N 5.77. *M* 239.27.

Ethyl 2-methyl-5*H*-chromeno[4,3-*b*]pyridine-3-carboxylate (25). Yield (0.19 g, 70%); colorless crystal (EtOH), mp: 110–112°C. IR spectrum, ν, cm^{-1}: 1721

(C=O). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.42 t (J = 8 Hz, 3H, CH_3), 2.91 s (3H, CH_3), 4.42 q (J = 8 Hz, 2H, CH_2), 5.2 s (2H, CH_2), 6.97–7.97 m (4H, ArH), 8.33 s (1H, CH-pyridine). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 14.32, 25.14, 61.21, 67.45, 117.19, 122.42, 122.46, 122.90, 123.78, 125.35, 132.19, 134.54, 150.34, 157.02, 160.03, 166.35. Mass spectrum: *m/z* 269 (100%). Calculated, %: C 71.36; H 5.61; N 5.20. $C_{16}H_{15}NO_3$. Found, %: C 71.43; H 5.52; N 5.32. *M* 269.30.

Ethyl 2-phenyl-5*H*-chromeno[4,3-*b*]pyridine-3-carboxylate (26). Yield (0.24 g, 72%); colorless crystals (EtOH), mp 130–132°C. IR spectrum, ν, cm^{-1}: 1721 (C=O). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.09 t (J = 8 Hz, 3H, CH_3), 4.81 q (J = 8 Hz, 2H, CH_2), 5.12 s (2H, CH_2), 7.09–7.81 m (9H, ArH), 8.21 s (1H, CH-pyridine). ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 21.22, 56.47, 61.15, 81.011, 116.11, 121, 122.46, 123.78, 126.41, 128.6, 128.8, 129.12, 132.32, 134.54, 136.51, 151.34, 157.02, 160.12, 166.35. Mass spectrum: *m/z* 331 (25%). Calculated, %: C 76.12; H 5.17; N 4.23. $C_{21}H_{17}NO_3$. Found, %: C 76.23; H 5.28; N 4.32. *M* 331.36.

2-(4-Chlorophenyl)-5*H*-chromeno[4,3-*b*]pyridine-3-carbonitrile (30). Yield (0.21 g, 74%); orange crystals (EtOH–dioxane), mp 225–227°C. IR spectrum, ν, cm^{-1}: 2212 (CN). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 5.22 s (2H, CH_2), 7.01–7.57 m (9H, ArH), 8.06 s (1H, CH-pyridine). Mass spectrum: *m/z* 318 (100%). Calculated, %: C 71.59; H 3.48, N,7.79. $C_{19}H_{11}ClN_2O$. Found, %: C 71.35; H 3.32; N 7.65. *M* 318.76.

2,5-Dihydro-2-oxo-1*H*-chromeno[4,3-*b*]pyridine-3-carbonitrile (31). Yield (0.17 g, 75%); orange crystals (EtOH–dioxane), mp 172–175°C. IR spectrum, ν, cm^{-1}: 3320 (NH), 1650 (C=O). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 5.07 s (2H, CH_2), 6.93 m (4H, ArH), 8.38 s (1H, CH-pyridine), 10.01 d (1H, NH, D_2O-exchangeable). ^{13}C NMR spectrum ($CDCl_3$), δ_H, ppm: 56.47, 81.01, 111.21, 116.11, 121, 122.46, 123.78, 129.12, 132.32, 13454, 151.34, 157.02, 166.35**.** Mass spectrum: *m/z* 224 (100%). Calculated, %: C 69.64; H 3.60; N 12.49. $C_{13}H_8N_2O_2$. Found, %: C 69.52; H 3.68; N 12.44. *M* 224.21.

ACKNOWLEDGMENTS

The project was financially supported by King Saud University, Vice Deanship of Research Chairs.

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